Pre-gravid Physical Activity and Reduced Risk of Glucose Intolerance in Pregnancy: The Role of Insulin Sensitivity

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Abstract

Objective—Pre-gravid physical activity has been associated with a reduced risk of gestational diabetes mellitus (GDM), although neither the types of exercise nor the physiologic mechanisms underlying this protective effect have been well studied. Thus, we sought to study the relationships between types of pre-gravid physical activity and metabolic parameters in pregnancy, including glucose tolerance, insulin sensitivity and beta-cell function.

Design/Patients/Measurements—851 women underwent a glucose challenge test (GCT) and a 3-hr oral glucose tolerance test (OGTT) in late pregnancy, yielding 4 glucose tolerance groups: (i) *GDM*; (ii) gestational impaired glucose tolerance (*GIGT*); (iii) abnormal GCT with normal glucose tolerance on OGTT (*abnormal GCT NGT*); and (iv) normal GCT with NGT on OGTT (*normal GCT NGT*). Pre-gravid physical activity was assessed using the Baecke questionnaire, which measures (i) total physical activity and (ii) its 3 component domains: work, non-sport leisure-time, and vigorous/sports activity.

Results—Glucose tolerance status improved across increasing quartiles of pre-gravid total physical activity ($p=0.0244$). Whereas neither work nor non-sport leisure-time activity differed between glucose tolerance groups, pre-gravid vigorous/sports activity was significantly higher in women with normal GCT NGT compared to women with (i) abnormal GCT NGT ($p=0.0018$), (ii) *GIGT* ($p=0.0025$), and (iii) *GDM* ($p=0.0044$). In particular, vigorous/sports activity correlated with insulin sensitivity (measured by IS_{OGTT}) ($r=0.21, p<0.0001$). Furthermore, on multiple linear regression analysis, pre-gravid vigorous/sports activity emerged as a significant independent predictor of IS_{OGTT} in pregnancy ($t=4.97, p<0.0001$).

Conclusions—Pre-gravid vigorous/sports activity is associated with a reduced risk of glucose intolerance in pregnancy, an effect likely mediated by enhanced insulin sensitivity.

Keywords

Physical Activity; Pregnancy; Gestational Diabetes; Insulin Sensitivity

INTRODUCTION

The diagnosis of gestational diabetes mellitus (GDM) frequently foreshadows the future development of type 2 diabetes (T2DM) in the years following the index pregnancy (1–3). This relationship likely reflects the pathophysiologic similarity between GDM and T2DM, insofar as both conditions are characterized by 2 main metabolic defects: (i) insulin resistance and (ii) pancreatic beta-cell dysfunction. Although the mechanistic basis of these defects has not been fully elucidated, it is now recognized that both GDM and T2DM may result from the pathologic interaction between underlying genetic susceptibility and acquired lifestyle factors, including dietary habits and physical inactivity (4–7). As such, there is currently considerable interest in the role of modification of diet and patterns of living as a means of attenuating inherited metabolic risk and thereby preventing the development of GDM and/or T2DM. Furthermore, in light of a recent meta-analysis that suggested that up to one third of parous women with T2DM may have a history of previous GDM (8), it follows that the prevention of GDM (through lifestyle modification) may be a particularly effective approach to combating the diabetes epidemic.

The role of diet in preventing GDM remains unclear, as studies to date have found little consistent association between nutritional factors and gestational glucose intolerance (6,9–12). In contrast, however, a series of recent reports have linked pre-gravid physical activity with a reduced risk of GDM (6,13–17). Although these reports have established this important association, it should be noted that neither the types of exercise nor the physiologic mechanisms underlying this protective effect have been well studied. An enhanced understanding of these issues potentially could inform the development of effective prevention strategies. In this context, we hypothesized that pre-gravid vigorous/sport activity may be particularly beneficial in relation to antepartum glucose homeostasis. Thus, in the current study, our objectives were to elucidate the relationships between specific domains of pre-gravid physical activity and metabolic parameters in pregnancy, including glucose tolerance, insulin sensitivity and beta-cell function.

RESEARCH DESIGN AND METHODS

This analysis was conducted in the setting of an ongoing observational study of early events in the natural history of T2DM, in which participating women recruited at the time of antepartum GDM screening undergo longitudinal metabolic characterization in pregnancy and the postpartum period (18,19). Standard obstetrical practice at our institution involves universal screening for GDM in all pregnant women at 24–28 weeks' gestation by 50g glucose challenge test (GCT) followed by, if the GCT is abnormal, referral for a diagnostic OGTT. In the study, healthy pregnant women are recruited either prior to or just after their

GCT. Regardless of the GCT result, all study participants then undergo a 3-hour 100g OGTT for determination of glucose tolerance status. All participants have provided written informed consent and the study protocol has been approved by the Mount Sinai Hospital Research Ethics Board. The current analysis is a cross-sectional evaluation of the study population at the time of the OGTT in pregnancy.

Evaluation of Study Participants in Pregnancy

On the morning of the OGTT, anthropometric measurements of height (to nearest 0.5 cm) and weight (to nearest 0.1 kg) were obtained using a medical scale. Data pertaining to medical, obstetrical, and family history were collected by interviewer-administered questionnaire. Pre-gravid physical activity in the year prior to pregnancy was assessed using the Baecke questionnaire, an established instrument that has been extensively validated in several populations, including women of childbearing age (20,21). The questionnaire was completed during the OGTT (ie. prior to knowledge of glucose tolerance status), with participants asked to report on their physical activity in the year prior to the pregnancy. The Baecke questionnaire measures (i) total physical activity and (ii) its 3 component domains: occupation-associated activity (*work index*); leisure-time activity not including sports (*non-sport leisure-time activity index*); and sport-related physical activity (*vigorous/sports index*). The work index quantifies the exertion related to occupational activities, such as sitting, standing, lifting, and walking, as well as associated effects on the individual (eg. fatigue, perspiration). The leisure-time index quantifies the exertion associated with non-sport recreational activities (such as walking and television viewing). The vigorous/sports index characterizes vigorous/sports activity with respect to intensity (using the updated Compendium of Physical Activities (22)), duration and frequency.

In conjunction with the GCT, the OGTT determined glucose tolerance status in pregnancy, as represented by the following 4 groups:

- i. **GDM**, as defined by National Diabetes Data Group (NDDG) criteria (23) (requires at least 2 of the following on the OGTT: fasting glucose ≥ 5.8 mmol/L, 1-hr blood glucose ≥ 10.6 mmol/L, 2-hr blood glucose ≥ 9.2 mmol/L, or 3-hr blood glucose ≥ 8.1 mmol/L);
- ii. **Gestational impaired glucose tolerance (GIGT)**, as defined by meeting only 1 of the above NDDG criteria;
- iii. **Abnormal GCT Normal Glucose Tolerance (NGT)**, as defined by having an abnormal 50g GCT (1-hour post-challenge plasma glucose ≥ 7.8 mmol/L) followed by NGT on the OGTT (defined by meeting none of the NDDG criteria);
- iv. **Normal GCT NGT**, defined as having a normal GCT followed by NGT on the OGTT

Laboratory Measurements and Physiologic Indices

On the day of the OGTT, participants arrived in the morning after overnight fast. Venous blood samples were drawn for measurement of plasma glucose and insulin at fasting and at 30-, 60- and 120-minutes and 180-minutes. Specific insulin was measured using the Roche

Modular system and the electrochemiluminescence immunoassay kit (Roche Diagnostics catalogue number 12017547122). This assay shows 0.05% cross-reactivity to intact human proinsulin and the primary circulating split form created by processing of the insulin pro-hormone (Des 31,32).

Glycemic measures included glucose tolerance status (as described above) and the total area-under-the-glucose-curve (AUC_{gluc}) during the OGTT (calculated using the trapezoidal rule applied to the 0-, 60-, 120- and 180-minute plasma glucose values). Insulin sensitivity was measured using the insulin sensitivity index (IS_{OGTT}) of Matsuda and DeFronzo (24). In pregnant women, IS_{OGTT} has been shown to exhibit stronger correlation with insulin sensitivity measured by euglycemic-hyperinsulinemic clamp than either Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) or Quantitative Insulin Sensitivity Check Index (25). Beta-cell function was assessed by the insulinogenic index divided by HOMA-IR (26,27). The insulinogenic index was calculated as the incremental change in insulin concentration during the first 30 minutes of the OGTT divided by the incremental change in glucose during the same time period (28). HOMA-IR was calculated as described by Matthews et al (29).

Statistical Analyses

All analyses were conducted using the Statistical Analysis System (SAS 9.1, SAS Institute, Cary NC). Continuous variables were tested for normality of distribution and natural log transformations of skewed variables were used, where necessary, in subsequent analyses. For each quartile of total physical activity score, continuous variables are presented as mean followed by standard deviation, if normally-distributed, or as median followed by interquartile range, if skewed, while categorical variables are presented as proportions. Univariate differences across the groups were assessed using Analysis of Variance (ANOVA) for continuous variables and χ^2 for categorical variables. Mean values of total physical activity score, work index, leisure-time index, and vigorous/sport index were compared across the 4 glucose tolerance groups by ANOVA. The odds ratio for abnormal glucose tolerance in pregnancy (GDM, GIGT, or abnormal GCT NGT) was determined for women above the 50th percentile for vigorous/sports index, compared to those below the 50th percentile. Univariate correlations between the domains of physical activity and metabolic parameters were assessed by Spearman correlation analysis. Multiple linear regression analysis was used to identify factors independently associated with the dependent variable IS_{OGTT} . Covariates of interest included age, weeks' gestation, pre-pregnancy BMI, weight gain in pregnancy preceding the OGTT, previous GDM, family history of T2DM, ethnicity (with Caucasian as reference group), and all 3 domains of pre-gravid physical activity (work index, non-sport leisure-time index, sport index). Covariates were considered to be retained in the model at a significance level of 0.05. Since the residual plot for the model with logarithmically-transformed IS_{OGTT} showed no difference compared to that of the model with IS_{OGTT} in original scale, we have presented the latter.

RESULTS

Characteristics of Study Population by Quartiles of Total Physical Activity

Table 1 shows the demographic, clinical and metabolic characteristics of the 851 study participants stratified by quartile of pre-gravid total physical activity score. There were no significant differences between the 4 groups with respect to age, pre-pregnancy BMI, weight gain per week of gestation, smoking exposure, parity, previous GDM, or family history of T2DM. Women in the 4th quartile underwent the OGTT slightly later (median 30 weeks' gestation) than women in the other three quartiles (each median 29 weeks) ($p=0.0034$). As total physical activity score increased, the proportion of Caucasian women rose while that of Asian women decreased ($p=0.0046$). Finally, as would be expected, total physical activity score and each of its 3 domains (work index, non-sport leisure-time index, vigorous/sport index) progressively increased across the 4 quartiles (each $p<0.0001$, respectively). The sport activities most frequently reported by women in the highest quartile of physical activity were the vigorous activities of running (24%), gym training (12%) and swimming (8%).

Turning to parameters of glucose metabolism, there were no significant differences between the quartiles with respect to GCT result, fasting glucose and AUC_{gluc} . Nevertheless, glucose tolerance status in pregnancy improved with increasing quartile of pre-gravid total physical activity ($p=0.0244$). In particular, as total physical activity increased, the prevalence of GDM decreased, while that of normal GCT NGT (ie. completely normal glucose tolerance) rose. Moreover, whereas insulinogenic index/HOMA-IR (beta-cell function) did not differ significantly between the groups, IS_{OGTT} (insulin sensitivity) increased in parallel with quartile of total physical activity ($p=0.0007$).

Domains of Physical Activity and Glucose Tolerance Status

To further elucidate the relationship between pre-gravid physical activity and antepartum glucose homeostasis, mean scores for each domain of physical activity were compared between the glucose tolerance groups. Mean total physical activity score ($\pm$ SD) was highest in women with normal GCT NGT (7.95 $\pm$ 0.12), followed in turn by the abnormal GCT NGT group (7.66 $\pm$ 0.06), GIGT (7.59 $\pm$ 0.1) and GDM (7.57 $\pm$ 0.1), respectively (overall $p=0.0491$) (Figure 1A). Amongst the component domains, mean work score ($p=0.9412$) and mean non-sport leisure-time score ($p=0.5666$) both did not differ across the four glucose tolerance groups (data not shown). Importantly, however, mean vigorous/sport activity varied considerably across the groups (overall $p=0.001$) (Figure 1). Indeed, pre-gravid vigorous/sports activity was significantly higher in women with normal GCT NGT compared to women with (i) abnormal GCT NGT ($p=0.0018$), (ii) GIGT ($p=0.0025$), and (iii) GDM ($p=0.0044$). Furthermore, upon median split of the study participants into 2 groups based on vigorous/sport index score, the odds ratio for abnormal glucose tolerance in pregnancy for women with higher levels of pre-gravid sports activity (ie. $>50^{\text{th}}$ percentile) was 0.53 (95% CI: 0.36–0.77), compared to their less sport-oriented peers. With adjustment for age, weeks' gestation, pre-pregnancy BMI, weight gain in pregnancy, family history of diabetes and ethnicity, this risk reduction remained significant with odds ratio 0.61 (95% CI: 0.39–0.96).

Domains of Physical Activity and Determinants of Glucose Homeostasis

Having demonstrated an association between pre-gravid physical activity (specifically vigorous/sport index) and glucose tolerance in pregnancy, we next sought to assess the relationships between the domains of physical activity and metabolic factors related to antepartum glucose homeostasis (measures of glycemia, beta-cell function and insulin sensitivity). On Spearman univariate correlation analysis, vigorous/sport index emerged as the domain that best correlated with metabolic parameters (GCT, AUC_{gluc} , IS_{OGTT}) (Table 2). Conversely, IS_{OGTT} was the metabolic parameter that best correlated with the physical activity measures (total physical activity, leisure-time index, vigorous/sport index). Accordingly, the strongest univariate association was between pre-gravid vigorous/sport index and IS_{OGTT} ($r=0.21$, $p<0.0001$)

As many factors may affect insulin sensitivity, we next sought to determine if pre-gravid sports activity was independently associated with antepartum IS_{OGTT} after adjustment for potential covariates. On multiple linear regression analysis, a model consisting of age, weeks' gestation, pre-pregnancy BMI, weight gain in pregnancy, family history of T2DM, previous GDM, ethnicity and the 3 domains of physical activity reconciled 30.0% of the variance of dependent variable antepartum IS_{OGTT} (Table 3). Importantly, pre-gravid vigorous/sports activity indeed emerged as a significant independent predictor of IS_{OGTT} ($\beta=0.60873$, $t=4.97$, $p<0.0001$). Significant negative determinants were pre-pregnancy BMI ($\beta=-0.23264$, $t=-14.62$, $P<0.0001$), weight gain in pregnancy ($\beta=-0.08406$, $t=-5.97$, $p<0.0001$), Asian ethnicity ($\beta=-1.36686$, $t=-5.10$, $p<0.0001$) and other non-white ethnicity ($\beta=-1.26223$, $t=-5.00$, $p<0.0001$), while age was a positive covariate ($\beta=0.06045$, $t=3.43$, $p=0.0006$). Neither work index nor non-sport leisure-time activity was significantly related to IS_{OGTT} .

Next, we tested for interaction amongst the model covariates. There were no significant interactions between vigorous/sport index and either age or weight gain in pregnancy (data not shown). A significant interaction, however, was detected between vigorous/sport index and pre-pregnancy BMI (interaction term: $t=-4.25$, $p<0.0001$). Indeed, the univariate association between pre-gravid vigorous/sport activity and IS_{OGTT} in pregnancy was stronger in lean women (pre-pregnancy BMI $<25 \text{ kg/m}^2$) ($r=0.22$, $p<0.0001$) than in those participants with pre-gravid BMI $\geq 25 \text{ kg/m}^2$ ($r=0.12$, $p=0.0364$).

Finally, to elucidate the role of intensity of sport activities, we calculated a mean intensity score for each participant, defined as the mean of the following construct calculated for each sport activity reported by the individual. This construct was the product of (i) the intensity code for the sport activity reported (as determined using the updated Compendium of Physical Activities (22)), (ii) the amount of time per week engaged in the activity, and (iii) the proportion of the year during which this activity was performed. Like the vigorous/sport index, on Spearman univariate analysis, this intensity score was significantly associated with IS_{OGTT} ($r=0.17$, $p<0.0001$). Furthermore, on multiple linear regression analysis, this intensity score also emerged as a significant independent predictor of IS_{OGTT} ($\beta=0.21899$, $t=3.97$, $p<0.0001$), after adjustment for age, weeks' gestation, pre-pregnancy BMI, weight gain in pregnancy, family history of diabetes, previous GDM, and ethnicity.

These data thus suggest that the intensity of pre-gravid vigorous/sport activity is positively associated with antepartum insulin sensitivity.

DISCUSSION

In this report, we demonstrate that physical activity in the year prior to pregnancy is associated with a reduced risk of GDM and that this relationship is specifically driven by vigorous/sports activity. Indeed, increased pre-gravid vigorous/sports activity was associated with a significantly reduced risk of any degree of glucose intolerance in pregnancy. Furthermore, increased pre-gravid vigorous/sports activity was independently associated with enhanced insulin sensitivity in late 2nd/early 3rd trimester. Taken together, these data support the value of improving insulin sensitivity in women at risk for GDM and suggest that pre-pregnancy vigorous physical activity within the year prior can provide a means of achieving this goal.

A series of recent reports have linked pre-gravid physical activity with risk reduction for GDM (6,13–17). In the Nurses Health Study II, women in the highest quintile of physical activity (specifically vigorous activity) had a ~20% risk reduction for the development of GDM (14). Similarly, in the Project Viva observational cohort, physical activity before pregnancy (again, particularly vigorous activity) was associated with a reduced risk of either GDM or any antepartum glucose intolerance (risk reductions of 44% and 24%, respectively, for vigorous activity) (15). Furthermore, in a cohort of 909 women, Dempsey and colleagues also found that leisure-time physical activity (ie. non-occupational) in the year prior to pregnancy correlated with a lower risk of GDM (13). Our findings of a protective effect of pre-gravid physical activity are thus consistent with these earlier reports, while extending this literature by identifying the specific contribution of vigorous/sports activity in this context. Moreover, as neither the work nor non-sport leisure-time activities of the study subjects are as likely to represent vigorous exertion as their sport activities (eg. as evidenced by the nature of the subjects' occupations), our findings regarding the specific role of sports exertion are likely consistent with the data from earlier studies describing vigorous activity. Accordingly, intensity of the exertion is likely the mechanism that links pre-pregnant sports activity with a reduced risk of antepartum glucose intolerance.

An important novel dimension of the current study is the evaluation of the relationships between pre-gravid physical activity and metabolic factors that determine glucose tolerance in pregnancy. Specifically, while not related to beta-cell function, pre-gravid vigorous/sport activity is shown to be associated with improved antepartum insulin sensitivity, thereby suggesting a possible mechanism underlying the GDM risk reduction. Interestingly, we demonstrate a differential effect of pre-pregnancy vigorous/sports activity on insulin sensitivity depending on body habitus, with lean women ($\text{BMI} < 25 \text{ kg/m}^2$) deriving much greater benefit (re insulin-sensitization) than women with $\text{BMI} \geq 25 \text{ kg/m}^2$ (although it is recognized that definitive commentary in this regard is precluded by the absence of data on exercise in pregnancy). This finding may provide an explanation for an earlier observation in Project Viva (15), where vigorous pre-pregnancy exercise significantly reduced the risk of abnormal glucose tolerance in pregnancy in lean women (adjusted odds ratio 0.56, 95% CI 0.36–0.88), but not in women with $\text{BMI} \geq 25 \text{ kg/m}^2$ (adjusted odds ratio 1.03, 95% CI

0.59–1.79). Taken together, these data support the idea that an improvement in insulin sensitivity with pre-gravid vigorous/sports activity may be contributing to the reduced risk of GDM.

It is well recognized that exercise training can improve insulin sensitivity by a variety of mechanisms, such as; (i) enhancing glucose uptake into skeletal muscle (ie. by increasing GLUT4 translocation), (ii) affecting proteins involved in insulin signal transduction (eg. AMP-activated protein kinase (AMPK) and the protein kinase B (Akt) substrate AS160), and (iii) increasing the oxidative capacity of skeletal muscle (by upregulating lipid oxidation and mitochondrial biogenesis) (30). In the current study, it is important to recognize that pre-pregnancy vigorous/sports activity correlated with insulin sensitivity in late 2nd/early 3rd trimester (ie. ~7 months later). This relationship is intriguing, when one considers that there are many factors that are known to affect insulin sensitivity, including genetic determinants, body habitus, and hormonal factors.^{5,26} Indeed, the effect of multiple factors is consistent with both (i) the relatively modest unadjusted Spearman univariate correlations observed between physical activity domains and IS_{OGTT} in Table 2 and (ii) the identification of several significant correlates of IS_{OGTT} on the multiple linear regression analysis (Table 3). Nevertheless, despite the effects of multiple factors, it is noteworthy that pre-gravid vigorous/sports activity still emerged as an *independent* determinant of antepartum insulin sensitivity, after adjustment for covariates (Table 3).

The mechanisms underlying this apparent later benefit of pre-gravid exercise are unclear. A likely possibility is that pre-pregnancy exercise patterns may carry on into pregnancy and thereby affect antepartum insulin sensitivity (a possibility that we cannot address in this study, as exercise patterns during pregnancy were not evaluated). Alternatively, the physiologic benefits of pre-gravid exercise may persist into pregnancy. In this context, it is possible that increased insulin sensitivity prior to pregnancy may enable better maintenance of insulin sensitivity in late pregnancy, thereby allowing for appropriate beta-cell compensation and the maintenance of normoglycemia. Such an effect may be particularly important in women at risk of GDM, since this patient population exhibits chronic insulin resistance that is believed to pre-date pregnancy (31,32). Indeed, as increased insulin resistance in 1st trimester (which largely reflects the pre-gravid state) predicts a higher risk of developing GDM later in pregnancy (33,34), it is plausible that improving insulin sensitivity prior to pregnancy would reduce GDM risk.

The insulin-sensitizing adipokine adiponectin is a potential candidate mediator in the relationship between pre-gravid physical activity, insulin sensitivity and risk of GDM. Specifically, low circulating levels of total adiponectin and its high-molecular-weight (HMW) form are related to both GDM and decreased insulin sensitivity (35–37). Exercise can increase both total and HMW adiponectin (38). It is therefore possible that pre-gravid physical activity raises total and HMW adiponectin levels and thereby improves insulin sensitivity and lowers risk of GDM. Consistent with this idea, it should be noted that low total adiponectin in 1st trimester (like insulin resistance) predicts subsequent GDM later in pregnancy (39). Similarly, the current data supports the value of improving insulin sensitivity in women at risk of GDM. Furthermore, following a pregnancy complicated by GDM, insulin-sensitization by either lifestyle modification or thiazolidinedione treatment

has been shown to significantly reduce the risk of developing T2DM(32,40). The current study extends this paradigm to the pre-gravid state, at which time it now emerges that insulin-sensitization via vigorous/sports activity may reduce the subsequent risk of GDM.

A limitation of this analysis is that the observational nature of the study precludes the exclusion of possible residual confounding by unmeasured factors, despite our having adjusted for several known factors associated with GDM and insulin sensitivity (including age, ethnicity, BMI, weight gain in pregnancy, family history of diabetes and previous GDM). The unmeasured variables include diet, socio-economic status and physical activity during the pregnancy, any of which may be acting upon the relationships reported herein. As such, definitive inference on causality cannot be made with this study. Nevertheless, this analysis is the first report to specifically link pre-gravid vigorous/sports activity with insulin sensitivity in pregnancy, a biologically very plausible association that reconciles several earlier observations, as noted above. Further study is warranted to address the specific biochemical mediators that may be relevant to this relationship.

In summary, physical activity in the year prior to pregnancy is associated with a reduced risk of GDM. This relationship is specifically driven by vigorous/sports activity, which is independently associated with enhanced insulin sensitivity in late pregnancy. Thus, taken together, these data suggest a model in which physical activity prior to pregnancy improves insulin sensitivity and reduces the risk of GDM. As such, these data support the value of improving insulin sensitivity in women at risk for GDM and suggest that vigorous physical activity can provide a means of achieving this goal.

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Figure 1.

Plot of mean vigorous/sport index, by glucose tolerance group in pregnancy (normal GCT NGT, abnormal GCT NGT, GIGT, GDM)

Table 1

Clinical and metabolic characteristics of study population stratified by quartiles of pre-gravid total physical activity score

	Lowest Quartile n=242	Second Quartile n=195	Third Quartile n=221	Fourth Quartile n=193	P
Age (yrs)	33.2 [4.1]	33.9 [4.0]	33.4 [4.6]	33.8 [5.5]	0.3567
Weeks' gestation at OGTT (wks)	29 [28–30]	29 [28–31]	29 [28–31]	30 [28–32]	0.0034
Pre-pregnancy BMI (kg/m ²)	24.1 [21.4–28.6]	24.2 [21.3–28.8]	23.0 [21.2–27.4]	23.1 [21.0–27.0]	0.0537
Weight gain per week (kg/wk)	0.3 [0.2–0.4]	0.3 [0.3–0.4]	0.3 [0.3–0.5]	0.4 [0.3–0.5]	0.0647
Smoking exposure:					0.3530
Never (%)	70	70	71	63	
Remote (%)	27	28	28	35	
Current (%)	3	2	1	2	
Parity:					0.2916
Nulliparous (%)	55	51	55	61	
One (%)	33	44	33	29	
Greater than one (%)	12	6	12	10	
Previous GDM/macrosomia (%)	5.0	7.7	4.1	4.7	0.5616
Family history of DM (%)	51.7	54.9	48.0	51.8	0.6761
Ethnicity:					0.0046
Caucasian (%)	68	75	74	79	
Asian (%)	18	12	13	8	
Other (%)	14	13	13	13	
Pre-gravid physical activity score	6.2 [0.6]	7.3 [0.2]	8.1 [0.3]	9.4 [0.7]	<0.0001
Work index	2.0 [0.4]	2.4 [0.5]	2.6 [0.6]	2.9 [0.6]	<0.0001
Leisure-time index	2.5 [0.4]	2.9 [0.5]	3.2 [0.5]	3.5 [0.5]	<0.0001
Vigorous/Sport index	1.6 [0.4]	2.1 [0.5]	2.4 [0.5]	3.0 [0.7]	<0.0001
<i>Glucose Metabolism</i>					
Glucose challenge test (mmol/L)	8.3 [1.3]	8.2 [1.4]	8.2 [1.3]	8.0 [1.4]	0.1150
Fasting glucose (mmol/L)	4.5 [0.5]	4.6 [0.5]	4.5 [0.6]	4.5 [0.6]	0.1671
AUC _{gluc} on OGTT	23.0 [3.4]	23.1 [3.7]	22.8 [3.9]	22.3 [3.6]	0.1960
Glucose tolerance status:					0.0244
Normal GCT NGT (%)	10.3	14.4	11.8	20.2	

	Lowest Quartile n=242	Second Quartile n=195	Third Quartile n=221	Fourth Quartile n=193	p
Abnormal GCT NGT (%)	48.8	47.7	48.9	47.7	
GIGT (%)	19.8	14.9	19.5	15.5	
GDM (%)	21.1	23.1	19.9	16.6	
Insulinogenic Index/HOMA-IR	10.2 [6.6–5.7]	9.9 [6.1–14.4]	10.3 [6.5 –16.9]	11.1 [6.4–16.7]	0.5412
IS _{OGTT}	3.8 [2.7–5.4]	4.2 [2.8–5.9]	4.6 [3.0–6.2]	4.9 [3.1–7.1]	0.0007

Data are presented as mean followed by standard deviation, with the exception of (i) weeks' gestation, pre-pregnancy BMI, weight gain/week, insulinogenic index/HOMA-IR and ISOGTT (presented as median followed by interquartile range) and (ii) smoking, parity, previous GDM, family history of DM, ethnicity and glucose tolerance status (presented as percentages).

p-values refer to overall differences across groups as derived from ANOVA analysis for continuous variables (parametric test for normally-distributed variables and non-parametric test for skewed variables) or χ^2 test for categorical variables

Spearman univariate correlations of glucose metabolism factors with overall physical activity score, and its components: (i) work index, (ii) leisure-time index, and (iii) vigorous/sports index

Table 2

	Physical Activity Score		Work Index		Leisure-time Index		Sport Index	
	r	p	r	p	r	p	r	p
Glucose challenge test	-0.09	0.0135	0	0.9035	-0.05	0.1544	-0.10	0.0024
Fasting glucose	-0.06	0.1066	0.05	0.1280	-0.07	0.0455	-0.08	0.0155
AUC _{gluc} on OGTT	-0.08	0.0261	0.03	0.3052	-0.04	0.1907	-0.11	0.0015
Insulinogenic Index/HOMA-IR	0.01	0.7607	-0.13	0.0004	0.04	0.2050	0.09	0.0104
IS _{OGTT}	0.14	<0.0001	-0.08	0.0218	0.13	0.0002	0.21	<0.0001

Bold indicates p<0.005

Table 3

Multiple linear regression analysis of dependent variable IS OGTT

Variable	Parameter Estimate	Standard Error	t value	p
Intercept	9.12806	1.30852	6.98	<0.0001
Age	0.06045	0.01865	3.43	0.0006
Weeks' gestation	-0.01933	0.03321	-0.58	0.5607
Pre-pregnancy BMI	-0.23264	0.01616	-14.62	<0.0001
Weight gain in pregnancy	-0.08406	0.01409	-5.97	<0.0001
Family history of diabetes	-0.27675	0.16884	-1.64	0.1016
Previous GDM	-0.52425	0.40064	-1.31	0.1911
Ethnicity:				
Asian ethnicity	-1.36686	0.26824	-5.10	<0.0001
Other non-white ethnicity	-1.26223	0.25236	-5.00	<0.0001
Work index	0.08081	0.13683	0.59	0.5550
Leisure-time index	-0.01266	0.15438	-0.08	0.9347
Vigorous/Sport index	0.60873	0.12247	4.97	<0.0001

model $r^2 = 30.0\%$